

POTASSIUM FLUORIDE  
AS A BASE IN ORGANIC REACTIONS  
SOLUBILIZED BY 18-CROWN-6

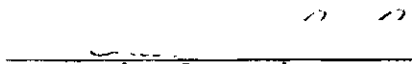
A THESIS  
Presented to  
The Faculty of the  
Division of Graduate Studies  
by  
Thomas Ray Henson

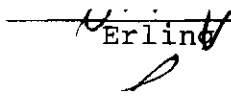
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POTASSIUM FLUORIDE  
AS A BASE IN ORGANIC REACTIONS  
SOLUBILIZED BY 18-CROWN-6

Approved:

  
\_\_\_\_\_  
Charles Liotta, Chairman

  
\_\_\_\_\_  
Erling Grovenstein

  
\_\_\_\_\_  
Leon Agnew

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## SUMMARY

Heterogeneous reactions were carried out in which potassium fluoride was solubilized in the polar and nonpolar aprotic solvents, acetonitrile and benzene, in the presence and absence of 18-crown-6, a solubilizing agent for potassium salts. The reactions studied were selected Michael, Knoevenagel, and alkylation reactions. In the Michael reactions ethyl cyanoacetate and diethyl malonate were the reactants with acrylonitrile and ethyl acrylate the substrates. In the Knoevenagel reactions the same reactants as the Michael reactions were used with the inclusion of malononitrile and benzaldehyde as the substrate. Cyclohexanone was also used as a substrate in the Knoevenagel reactions for one reaction. The alkylations were carried out with diethyl malonate as the reactant and benzyl bromide, benzyl chloride, and methyl iodide as substrates. With only catalytic quantities of 18-crown-6 present the reactivity of the fluoride anion as a base was enhanced. The reaction times were shorter and the product yields were better or at least equivalent to reactions with no 18-crown-6. The product yields were also comparable to yields obtained by other synthetic methods.

Three unique complexes with 18-crown-6 were also isolated. Cyanogen bromide, malononitrile, and succinonitrile was found to form two to one (nitrile to 18-crown-6 molar

ratio) complexes. Of these, the malononitrile and succinonitrile complexes were the most stable melting at 129-130°C and 83-84°C, respectively. Small shifts in the infrared region of the nitrile moiety was noted with complexation, as well as, small shifts in the  $^{13}\text{C}$ -NMR for 18-crown-6 and nitrile moieties with complexation.

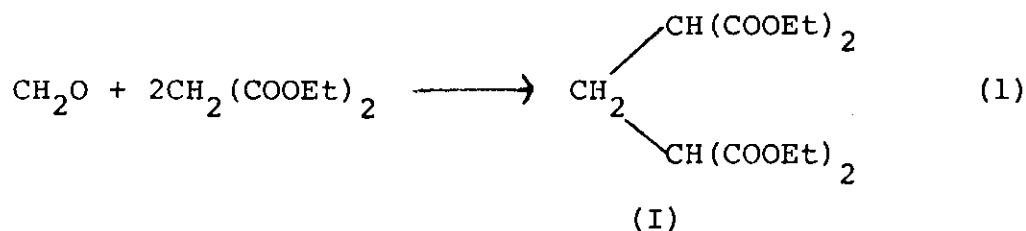


## CHAPTER I

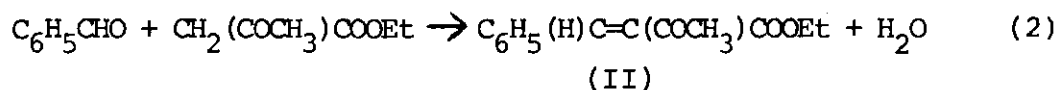
### INTRODUCTION

#### Condensation Reactions

The Knoevenagel condensation was initially concerned with the reaction of formaldehyde with active methylene nucleophiles in the presence of basic catalysts yielding bis products as (I).<sup>1</sup> In 1896 Knoevenagel reported ethyl acetoace-



tate and benzaldehyde condensed in the presence of piperidine at low temperatures to yield ethyl benzylideneacetoacetate (II)<sup>2</sup>. The scope and utility of the Knoevenagel condensation



has since been expanded.

The Knoevenagel condensation is defined as the reaction of active methylene compound with ketones or aldehydes brought about by basic catalysis. The active methylene compounds are characterized by the presence of electron-withdrawing groups, usually two. The most common activating

groups are the cyano, nitro, acyl, and carboalkoxy. These groups are necessary to increase the acidity of the methylene group by providing resonance stabilization of the anionic conjugate base. The primary product of the condensation is usually an unsaturated compound, although in some cases a Michael condensation can occur with an additional mole of active methylene compound to yield a bis compound as (1).

A consistent mechanism for the wide range of Knoevenagel condensations in a single unified mechanism seems impossible. There is evidence for the existence of two mechanisms depending on the type of base used. The intermediacy of imines and Schiff bases with the use of primary amines and ammonia is favored.<sup>3-6</sup> However, in polar solvents the Hann and Lapworth mechanism is favored, wherein the base removes a proton from the active methylene compound. The resonance stabilized anion then adds to the carbonyl forming an intermediate hydroxyl compound.<sup>7-10</sup>

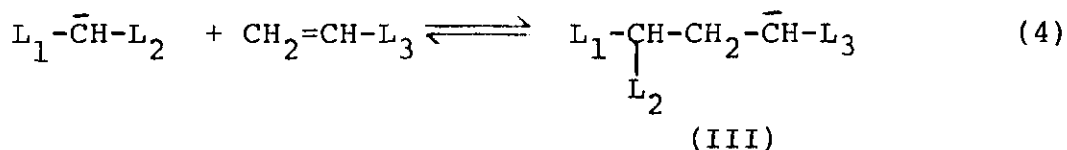
Cope<sup>11,12</sup> found that amine salts of organic acids in the presence of acetic acid were better catalysts than free bases. The continuous removal of water from the condensation was also shown to increase the yields. The need for small amounts of acid to be present during the condensation has been substantiated.<sup>13</sup> The temperature and choice of catalyst needed to carry out the condensation depends on the nature of the reactants.

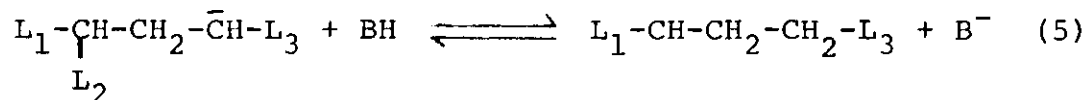
The most commonly used catalysts in the Knoevenagel

condensation have been pyridine, piperdine, and ammonium or amine acetates. Other catalysts employed besides these are amino acids, basic resins, sodium hydroxide, acetic anhydride, zinc chloride, titanium tetrachloride and potassium fluoride.<sup>14</sup>

The Michael condensation, unlike the Knoevenagel condensation for carbon-carbon double bond formation, is a process for alkylation of a carbon-carbon double bond. The condensation is the nucleophilic addition of an anion, usually resonance stabilized, to a carbon-carbon double bond of an  $\alpha$ ,  $\beta$ -unsaturated aldehyde, ketone, nitrile, or carboxylic acid derivatives. These unsaturated compounds are generally referred to as Michael acceptors, characterized by the presence of an electron-withdrawing group capable of stabilizing a carbanionic intermediate of the reaction. The condensation takes place under the influence of basic reagents.<sup>15</sup> When acrylonitrile is the Michael acceptor, the process is commonly known as cyanoethylation.<sup>16</sup>

The mechanism of the Michael condensation has been established.<sup>17-21</sup> A general representation of the reaction is as follows, where  $L_1$ ,  $L_2$ ,  $L_3$  represent labilizing groups.





$L_1$ ,  $L_2$  or both may be  $-\text{COOR}$ ,  $-\text{COR}$ ,  $-\text{CN}$ ,  $-\text{CONH}_2$ ,  $-\text{NO}_2$ ,  $-\text{SO}_2\text{R}$ , or  $-\text{CHO}$  and  $L_3$  may be  $-\text{COOR}$ ,  $-\text{COR}$ ,  $-\text{CN}$ ,  $-\text{CONH}_2$ ,  $-\text{NO}_2$ , or  $-\text{SO}_2\text{R}$ . The rate-limiting reaction step (4) is the formation of a new carbon-carbon bond. The carbanionic intermediate (III) is resonance stabilized by  $L_3$ . From the mechanism three conclusions can be reached: 1) the base for generating the anion is regenerated, therefore only a catalytic amount of base is required, 2) the Michael process is reversible requiring an excess of active methylene compound, and 3) due to the reversibility and stabilization of the carbanionic intermediate (III) side reactions are possible. Consequently, the Michael condensation is effected using the mildest possible conditions, weak basic catalyst, low temperature, and short reaction times.

The catalysts most commonly used in the Michael condensation have been piperidine, pyridine, triethylamine, potassium hydroxide, benzyltrimethylammonium hydroxide (triton B), sodium hydroxide, sodium ethoxide, potassium *t*-butoxide, sodium hydride, or other metal amides. Besides these, other less frequently used catalysts have been acidic catalysts such as boron trifluoride, zinc chloride, and sulfur dioxide, as well as, the basic catalysts calcium hydride, sodium cyanide, potassium carbonate, sodium triphenylmethide, and

potassium fluoride.<sup>15</sup>

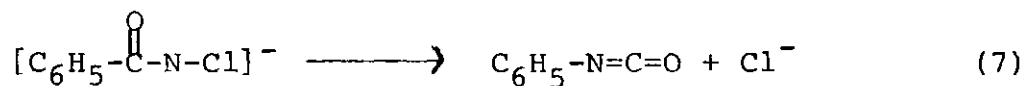
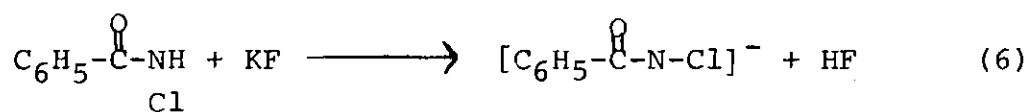
#### Potassium Fluoride as a Base

The use of fluoride as a basic catalyst in organic reactions is only a relatively recent development. The ability of fluoride ions to act as a base can be rationalized. The fluoride ion is much smaller than other halide ions, therefore, increasing the charge to volume ratio, leading to a greater effect at centers of positive charge. The result of this effect means fluoride would have an increased affinity for a proton. This fact is established from data showing fluoride ions, or bonded fluorine, forming stronger hydrogen bonds than other ions.<sup>23,24</sup> Potassium fluoride has mainly been used as a fluorinating agent in organic chemistry.<sup>25</sup>

Nesmeyanov<sup>26</sup> found that upon heating trichloroacetic acid in nitrobenzene with dry potassium fluoride, a gas evolved and chloroform formed in 70% yield instead of the expected trifluoroacetic acid. Other carboxylic acids were also found to decarboxylate, with adipic and pimelic acids yielding cyclopentanone and cyclohexanone, respectively. The decarbonylation of chloral was also found to occur spontaneously in refluxing, absolute ethanol. Rand, et al.,<sup>27</sup> showed the initial step in the decarboxylation of adipic acid with potassium fluoride to be the removal of the acid proton by fluoride forming the monocarboxylate anion. This anion decarboxylates forming a carbanion which then cyclizes and elim-

inates hydroxide.

Rand, et al.,<sup>28,29</sup> found that N-chlorobenzamide in benzene undergoes a Hofmann reaction in the presence of anhydrous potassium fluoride. The mechanism for the reaction was consistent with fluoride removing the amide proton, followed by a Hoffmann-type rearrangement giving phenyl isocyanate. The phenyl isocyanate then adds one mole of the N-chlorobenzamide with hydrolysis yielding the N-benzoyl-N'-phenylurea in high yields. The yield of the product was found to be dependent upon the concentration of potassium fluoride, two equivalents of the starting amide to one equivalent of potassium fluoride.



Aoyama<sup>30-33</sup> has used anhydrous potassium fluoride as a base in the Knoevenagel condensation under a variety of conditions. The most commonly used solvents were diethyl ether or ethanol and in many cases no solvent. Aoyama condensed ethylcyanoacetate with various aromatic aldehydes, ethylacetoacetate and diethyl malonate with aliphatic aldehydes, acetone with ethylcyanoacetate, and ethylcyanoacetate with aliphatic ketones. Malonic esters and acetoacetic ester failed to react with the aliphatic ketones under these conditions. However, Sakweai<sup>34</sup> was able to condense ethyl ma-

lonate and ethyl acetoacetate with aliphatic aldehydes. The yields of the reactions ranged from 20 to 80% and usually required external heating.

Rand<sup>35,36</sup> showed potassium fluoride to act as a basic catalyst in the Knoevenagel condensation of benzaldehyde or cyclohexanone with malononitrile, ethyl cyanoacetate, and diethyl malonate. The kinetics of the cyclohexanone and ethyl cyanoacetate condensation in ethanol was studied spectrophotometrically. The kinetics indicated a third-order reaction, first order in the fluoride. From kinetic and conductance data the first step of the condensation was postulated as the metal fluoride ion pair abstracting a proton from the



active methylene compound forming a carbanion.

The use of potassium fluoride as a catalyst in the Michael condensation was found successful.<sup>37-42</sup> Ethanol was the common solvent or no solvent at all. The condensations generally required some external heating, with temperatures ranging from 40°C to refluxing ethanol temperature. The time for the condensations ranged from one hour to, as much as, forty-eight hours giving yields from 40 to 80%.

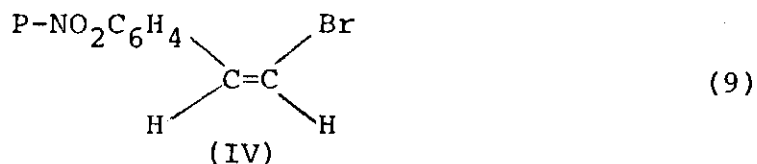
When donors of the Michael condensation, such as ethylnitroacetate, nitroketones with a CH<sub>2</sub>NO<sub>2</sub> group, and gem-dinitroalkanes, are used with potassium fluoride as the base, a double salt is formed, for example, gem-dinitroethane formed

$C_2H_4N_2O_4K_2F_2$ . The double salts were found to be formed by compounds with a  $pK_a$  less than 7. The double salts also gave the normal Michael product when an acceptor was present, except for the nitroketones which gave condensation products of acceptors reacting with nitromethane. The formation of such double salts supports the assumption that the Michael reaction with potassium fluoride proceeds via formation of a carbanion.<sup>43</sup>

Potassium fluoride has also been used to catalyze aldol condensations,<sup>44</sup> Michael-Knoevenagel dehydration sequences,<sup>45,46</sup> and polyfluoroalkylation.<sup>47</sup> Tetraalkylammonium fluorides have also been used to provide a homogenous system, whereby the fluoride acts as a base, to explore elimination reaction mechanisms in polar, aprotic solvents.<sup>48-52</sup> However, the tetraalkylammonium fluorides have been found to be unstable at room temperature and higher temperatures degrading to ethylene, triethylamine and hydrogen fluoride.<sup>53</sup>

Naso and Ronzini found the addition of 2,5,8,15,18,21-hexaoxatricyclo [20.4.0.0<sup>9,14</sup>] Hexacosane, commonly termed dicyclohexyl-18-crown-6 [see later discussion for structure] increased the solubility of potassium fluoride in acetonitrile, DMF, and butyl cellulose (ethylene glycol mono-n-butyl ether). This increase in the solubility of potassium fluoride also accompanied an increase in the reactivity of the fluoride as a base in the formation of acetylene from structure (4). The greatest reactivity was found in acetonitrile





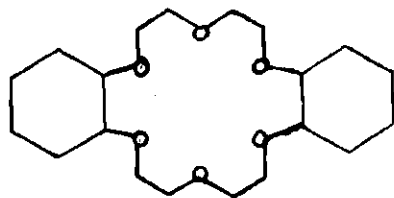
with 53 to 71% conversion to acetylene with the crown present and 0% conversion with no crown present. Less of an effect was found to occur in DMF and butyl cellulose although greater conversions were obtained when the crown was present.<sup>54</sup>

#### Crown Ethers

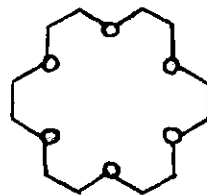
Pedersen<sup>55-61</sup> first isolated and described the macrocyclic polyethers. The most notable discovery was the ability of the polyethers to complex the alkali metal cations and in some cases to form stable complexes. Pedersen described many of these initial complexes and attributed their formation to ion-dipole interactions between the cation and the negatively charged oxygen atoms which are symmetrically arranged in the polyether ring.

Pedersen also gave these macrocyclic polyethers the trivial nomenclature of "crown" compounds. The trivial names are assigned on the following basis: 1) the number and kind of hydrocarbon rings, if present, 2) the total number of atoms in the polyether ring, 3) the class name, crown, and 4) the number of oxygen atoms in the polyether ring. The placements of the hydrocarbon rings and oxygen atoms are as symmetrical as possible, and the exceptions are indicated by asym. For example, structure (V) has the systematic name 2,5,

8,15,18,21-hexaoxatricyclo[20.4.0.0<sup>9,14</sup>] hexacosane or di-cyclohexyl-18-crown-6 referred to previously by trivial



V



VI

nomenclature. Structure (VI) has the systematic name 1,4,7,10,13,16-hexaoxacyclooctadecane or 18-crown-6 by the trivial nomenclature. Structure (VI) will be referred to as 18-crown-6 throughout the remainder of the thesis.

New and improved synthesis have recently been published for various crown ether systems,<sup>62-63</sup> including 18-crown-6<sup>64</sup> 12-crown-4,<sup>65</sup> and 15-crown-5.<sup>65</sup> Besides the oxygenated crown ethers, crown ethers containing other hetero-atoms have been synthesized for investigation.<sup>66-71</sup> Crown ethers have also been prepared in polymeric form with molecular weights ranging from 30,000 to 100,000 by radical or anionic initiation reactions.<sup>72-75</sup>

The ability of the crown ethers to complex alkali metal cations has directed much effort to exploring these interactions. With the formation and isolation of solid complexes, x-ray crystallography was used to elucidate these structures.<sup>76-88</sup> The solution chemistry of crown ethers

interacting with metal cations has been studied by colorimetry,<sup>89-91</sup> potentiometry,<sup>92</sup> distribution equilibria,<sup>93</sup> visible and ultraviolet spectroscopy,<sup>94-96</sup> ESR,<sup>97</sup> and paper chromatography.<sup>98</sup> Other complexes of crown ethers besides the metal cation complexes have also been reported.<sup>99-101</sup>

Crown ethers have been used as addends to investigate the ion-pair processes of fluorenyl salts in solution. The crown ethers were found to increase ion-pair dissociation in a variety of solvents by converting contact ion-pairs to solvent-separated ion pairs.<sup>102-114</sup> Because of this effect, crown ethers have also been used as addends in elimination reactions as a definitive means of determining the effect of base association in these reactions.<sup>115-119</sup>

Few synthetic applications of the crown ethers have been reported. Sam and Simmons<sup>120</sup> solubilized potassium permanganate in benzene with concentrations as high as 0.03 Molar using dicyclohexyl-18-crown-6. Such a solution was found capable of oxidizing organic substrates as olefins, alcohols, aldehydes, and alkylbenzenes under mild conditions in excellent yields. Sam and Simmons<sup>121</sup> also used dicyclohexyl-18-crown-6 to solubilize potassium bromide and iodide in acetone to carry out nucleophilic substitutions on n-butyl brosylate. Potassium methoxide was shown also to increase in reactivity when dicyclohexyl-18-crown-6 was present. Liotta and Harris<sup>122</sup> solubilized potassium fluoride with 18-crown-6 in benzene and acetonitrile. This "naked" fluoride showed

marked activity to act as a nucleophile and base under mild conditions. Liotta<sup>123,124</sup> also found potassium acetate and potassium cyanide to have increased reactivity in acetonitrile in the presence of 18-crown-6.

Therefore, the purpose of the work presented in this thesis was to investigate the ability of "naked" fluoride ions to act as a base in polar and nonpolar aprotic solvents, acetonitrile and benzene, in the presence of 18-crown-6. The investigation consisted of running selected Michael, Knoevenagel, and alkylation reactions in the presence and absence of 18-crown-6 comparing reaction times and products isolated. The formation of three novel non-metallic 18-crown-6 complexes is discussed.

## CHAPTER II

## EXPERIMENTAL

All boiling points and melting points reported in this thesis are uncorrected and recorded in degrees centigrade. Infrared spectrum were obtained on a Perkin-Elmer 237B grating infrared spectrophotometer as thin liquid films (neat or  $\text{CCl}_4$ ) or as potassium bromide pellets using the  $1601.4\text{ cm}^{-1}$  absorption of polystyrene as a reference. NMR data were obtained on a Varian A60D or a Varian T60 spectrometer. Mass spectra were obtained on either a Varian M66 or a Hitachi Perkin-Elmer RMV-7L [bought by funds provided by National Science Foundation] spectrometers. Glpc work was carried out on a Varian Model 90P Gas Chromatograph with thermal conductivity detector and helium as carrier gas. Elemental microanalysis was performed by Atlantic Microlab, Inc., Atlanta, Georgia.

Chemicals

Acetonitrile (Fisher and Aldrich) was used without further purification. Benzene (Fisher) was distilled from sodium (2-5 g. per liter) under nitrogen collecting the fraction  $80.1-81^\circ\text{C}$ . Acrylonitrile (Fisher) was purified by the method of Fieser<sup>125</sup> and stored in a brown bottle and used without further purification. Ethyl acrylate (Eastman) was distilled under reduced pressure ( $< 1\text{ mm}$ ) and collected in a

round bottom flask, immersed in a dry ice/acetone bath and stored in a brown bottle in the refrigerator. Benzaldehyde (Fisher) was distilled with the colorless fraction collected, b.p. 178-180°C (740 mm) [lit.<sup>126</sup> b.p. 179.1 (760 mm)] and stored in a brown bottle in refrigerator. Ethyl Cyanoacetate (Eastman) was used without further purification. Diethyl Malonate (Fisher) was used without further purification. Malononitrile (Fisher) was distilled, b.p. 63-67°C (0.1 mm) [lit.<sup>127</sup> b.p. 223-224°C (760 mm)] and stored in a brown bottle in the refrigerator, whereby the material solidified, m.p. 31°C [lit.<sup>127</sup> m.p. 31.7°C]. Diethyl ether (Fisher) for extractions was used without further purification.

Potassium fluoride (ROC/RIC) used in these reactions was dried in an oven at 120°C for 12 hours. The potassium fluoride was then finely powdered in a hot mortar and transferred to a hot 500 ml. beaker. The potassium fluoride was allowed to dry for 12 additional hours before usage. The powdered potassium fluoride was then stored in the oven at 120°C at all times.

1,4,7,10,13,16-Hexaoxacyclooctadecane (18-crown-6)

18-crown-6 was prepared by the method of Cram, Liotta, et al.<sup>64</sup> A five-liter, three necked flask equipped with a mechanical stirrer and water-cooled bearing, a reflux condenser, and a 500 ml. dropping funnel, was charged with 230 g. of triethylene glycol (Matheson, Coleman and Bell 1.5 moles)

in 1000 ml. THF (Fisher). Potassium hydroxide (218 g. Fisher, 85% pellets) was dissolved in water (120 ml. distilled) and added in one portion to the stirred triethylene glycol mixture. After 30 minutes of stirring at ambient temperature (solution slowly darkens), a solution of 280 g. of 1,8-dichloro-3,6-dioxaoctane (Eastman practical, 1.5 moles) in 200 ml. THF was added in a thin stream to the stirred reaction mixture. With the addition completed, the mixture was heated to reflux for 15 hours. After this time, the solution was noted to be discolored and solid potassium chloride was present. The bulk of the solvent was removed on a rotary evaporator. The residual oil and solid was then stirred with a mechanical stirrer with a liter of methylene chloride, filtered, and dried over  $\text{MgSO}_4$ . This solution was filtered and concentrated on a rotary evaporator and distilled under a vacuum. After an initial forerun boiling 25-127°C (0.2 mm), crude crown ether (140 g., 35%) was collected, b.p. 128-150°C (0.2 mm). This material was purified through the acetonitrile complex. The crude crown was placed in a 250 ml. Erlenmeyer flask and 200 ml. of acetonitrile was added. The resulting slurry was heated until all the material dissolved. Then a magnetic stirring bar was added and the solution was stirred vigorously. A drying tube (Drierite) was put on the flask's top. As the solution cooled to room temperature, fine, white crystals of the crown ether/acetonitrile complex were formed. The flask was further cooled in an ice/acetone

bath to effect complete precipitation. The crown ether/acetonitrile complex was filtered and transferred to a 240 ml. round bottom flask. A magnetic stirring bar was added to the flask which was also equipped with a vacuum take-off and heating mantle. The acetonitrile was removed under a vacuum (0.3 to 0.1 mm) over a period of six hours with slight warming (Ca.  $40^{\circ}$ ). The pure crown ether (66 g., 45%) solidified on cooling and was sealed in the round bottom flask under  $N_2$ . The pure 18-crown-6 ether melted at  $36-38^{\circ}C$  [lit.<sup>63</sup> m.p.  $39-40^{\circ}$ ], showed only a singlet at  $\delta$  3.5 in the NMR ( $CCl_4$ , internal TMS) and ir absorptions (neat) at 2875 (alkane C-H), 1450 and 1350 (alkane C-H), and  $1120\text{ cm}^{-1}$  (ether C-O).

### Michael Condensations

#### Acrylonitrile and Ethylcyanoacetate Condensation

I. Into a 25-ml. volumetric flask, 6.25 g. (0.055 moles, 2.2 M) of ethylcyanoacetate was directly weighed and diluted to the mark with addition of acetonitrile (Fisher). Into a second 25-ml. volumetric flask, 2.65 g. (0.05 moles, 2.0 M) of acrylonitrile (Fisher) was directly weighed and diluted to the mark with addition of acetonitrile (Fisher). The ethylcyanoacetate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer. To the ethylcyanoacetate solution, 1.30 g. (0.0049 moles, 0.098 M) of 18-crown-6 was added and allowed to stir for five minutes.



Then 3.2 g. (0.055 moles) of hot, dry potassium fluoride was added to the ethylcyanoacetate solution and allowed to stir for five minutes. The acrylonitrile solution was slowly added by syringe over a five-minute period and the reaction slowly heated to 45°C during this time. The solution was cooled in an ice-water bath to a temperature of 30°C and removed. After ten minutes of reaction time, a sample of the reaction mixture was withdrawn and its NMR run. Vinyl proton resonance corresponding to acrylonitrile was not found in the NMR spectrum. The reaction mixture was stirred four hours and no vinyl protons were found in the NMR spectrum of the solution during this time. After four hours, the reaction mixture was poured into 250 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel. The organic layer was separated and the aqueous phase extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under vacuum, and ether removed by rotary evaporator. This left an oil which could not be distilled. Only a low boiling material was removed and shown to be ethylcyanoacetate (2 g.). The pot material was removed and the material slowly solidified. The solid material after sublimation in vacuo amounted to 9.4 g (86%) of  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile: m.p. 36-37°C [lit.<sup>128,129</sup> m.p. 38°C]; infrared absorption (KBr) at 2250  $\text{cm}^{-1}$  (nitrile  $\text{-C}\equiv\text{N}$ ) and 1740  $\text{cm}^{-1}$  (ester  $\text{C=O}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  4.40 (2H quartet,

--CH<sub>2</sub>-Me), at  $\delta$  2.8-1.8 (8H multiplet, NC-CH<sub>2</sub>-CH<sub>2</sub>-), and at  $\delta$  1.36 (3H triplet, CH<sub>3</sub>-); and mass spectrum m/e abundant fragments 174, 107, 68, 54, 41, and 27. No polymeric material was found.

Similarly, the same reaction was run in the absence of 18-crown-6. During the initial four hours of the reaction, NMR's of the reaction mixture showed a steady decline in the amount of acrylonitrile in the mixture. The mixture was stirred four additional hours. After the work up, as above, 8.8 g. (80%) of  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile was collected.

II. Into a 25-ml. volumetric flask, 6.25 g. (0.055 moles, 2.2 M) of ethylcyanoacetate was directly weighed and diluted to the mark with addition of acetonitrile. Into a second 25-ml. volumetric flask, 5.30 g. (0.1 moles, 4.0 M) of acrylonitrile was directly weighed and diluted to the mark with acetonitrile. The ethylcyanoacetate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer. To the ethylcyanoacetate solution 1.30 g. (0.0049 moles, 0.098 M) of 18-crown-6 was added and allowed to stir for five minutes. Then 3.2 g. (0.055 moles) of hot, dry potassium fluoride was added to the ethylcyanoacetate and allowed to stir for five minutes. The acrylonitrile solution was slowly added by syringe over a seven-minute period and the reaction slowly heated to 45° C during this time. The

flask was immersed in an ice-water bath, cooled to a temperature of 30° C and removed. The temperature rose to 35° C again but then slowly dropped to 25° C after one half hour. The solution was also a slight yellow in color. After ten minutes of reaction time, a sample of the reaction mixture was withdrawn and its NMR was taken. Vinyl proton resonance corresponding to acrylonitrile was not found in the NMR spectrum. The reaction mixture was stirred for one hour and no vinyl proton resonance was found in the NMR spectrum of the solution during this time. The reaction mixture was poured into 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel. The organic layer was separated and the aqueous phase extracted twice with 300 ml. of diethyl ether. The organic layer and ether extract were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and ether removed by rotary evaporator, leaving a viscous oil. The oil was left in the round bottom flask which was used for rotavaporation and equipped with a vacuum take-off. Complete removal of solvents in vacuo at ice bath temperatures gave a light, brown waxy solid. The solid after sublimation in vacuo amounted to 9.2 g. (83%) of  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile; m.p. 36-37° C [lit.<sup>128</sup> m.p. 38°, m.p. 37° C<sup>129</sup>].

Similarly, the same reaction was run in the absence of 18-crown-6. The decrease in acrylonitrile was followed by NMR over a 40-hour period with a slow but steady decline in acrylonitrile in the mixture. The mixture was stirred for an

additional three hours. After the work up, as above, 9.6 g. (84%) of  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile (m.p. 35-36° C) was collected.

III. Into a 25-ml. volumetric flask, 6.25 g. (0.055 moles, 2.2 M) ethylcyanoacetate was directly weighed and diluted to the mark with the addition of acetonitrile (dried over  $P_2O_5$  under  $N_2$ ) under  $N_2$  by a canulla. Into a second 25-ml. volumetric flask, 5.30 g. (0.1 moles, 4.0 M) acrylonitrile was directly weighed and diluted to the mark with the addition of acetonitrile under  $N_2$  by a canulla. A three necked 100-ml. round bottom flask equipped with a stirring bar, ground glass stopper, and rubber septum was charged with 1.30 g. (0.0049 moles, 0.098 M) 18-crown-6 and 3.2 g. (0.055 moles) hot, dry potassium fluoride. The flask was sealed with a rubber septum and flushed with  $N_2$ . The ethylcyanoacetate solution was transferred to the round bottom flask under  $N_2$  by canulla and stirred five minutes. The acrylonitrile solution was slowly added by syringe over a ten-minute period. The temperature rose quickly to 40° C and the flask was immersed in an ice-bath until the temperature dropped to 30° C. The flask was removed and procedure followed until the temperature stabilized below 35° C. After ten minutes of reaction time, a sample was withdrawn and its NMR spectrum taken. Vinyl proton resonance corresponding to acrylonitrile was not present. The reaction mixture was stirred four hours and then added to 100 ml. of water. The aqueous mixture was poured into a sep-

aratory funnel. The organic layer was separated and the aqueous phase extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed by rotary evaporator to give an oil. The oil solidified upon cooling in the refrigerator. The solid after sublimation in vacuo amounted to 10 g. (90%) of  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile (m.p.  $36^\circ \text{C}$ ).

#### Acrylonitrile and Diethylmalonate Condensations

I. Into a 25-ml. volumetric flask, 8.80 g. (0.055 moles, 2.2 M) of diethyl malonate was directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 25-ml. volumetric flask, 5.30 g. (0.1 moles, 4.0 M) of acrylonitrile was directly weighed and diluted to the mark with acetonitrile. The diethyl malonate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum and thermometer. To the diethyl malonate solution 1.30 g. (0.0049 moles, 0.098 M) of 18-crown-6 was added and allowed to stir for five minutes. The 3.20 g. (0.055 moles) of dry, hot potassium fluoride was added to the diethyl malonate and allowed to stir for five minutes. The acrylonitrile solution was slowly added by syringe over a five-minute period and the reaction slowly heated to  $41^\circ \text{C}$  during this time. The flask was immersed in an ice-water bath, cooled to a temperature of  $30^\circ \text{C}$ , and removed. The temperature increased again to

38° C but slowly dropped over two hours to 25° C. After ten minutes of reaction time a sample of the mixture was withdrawn and its NMR was taken. Vinyl proton resonance corresponding to acrylonitrile was found. The decrease in the acrylonitrile was followed by NMR over a three and one-half hour period at which time no vinyl proton resonance was found. The solution was allowed to stir overnight an additional nine and one-half hours. The reaction mixture was poured into 100-ml. of water and stirred. The aqueous mixture was poured into a separatory funnel. The organic layer was separated and the aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator. This left an oily material which solidified. The solid after sublimation in vacuo amounted to 10.8 g. (81.8%) of  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile; m.p. 56-57° C [lit.<sup>130,131</sup> m.p. 61° C]; infrared absorption (KBr) at 2250  $\text{cm}^{-1}$  (nitrile-- $\text{C}\equiv\text{N}$ ) and 1730  $\text{cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks ( $\phi$ - $\text{d}_6$ , internal TMS) at  $\delta$  4.05 (4H quartet,  $-\text{CH}_2-\text{Me}$ ), at  $\delta$  2.2-1.8 (8H multiplet,  $\text{NC}-\text{CH}_2-\text{CH}_2-$ ) and at  $\delta$  0.96 (6H triplet,  $\text{CH}_2-$ ); and mass spectrum, m/e abundant fragments 221, 173, 154, 108, 69, and 41.

Similarly, the same reaction was run in the absence of 18-crown-6. The decrease in acrylonitrile was followed by NMR over a 121 hour period with a slow decrease in acrylonitrile in the mixture. After passage of the 121 hours of reaction time, the reaction mixture was poured into 100-ml. of

water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The remaining aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed by rotary evaporator. There remained an oil which did not solidify on cooling in the freezer. The oil after distillation yielded 5.9 g. (0.037) b.p.  $40^\circ \text{C}$  (0.1 mm) of diethyl malonate and 2.1 g. (54%, based on recovered diethyl malonate) ethyl  $\alpha$ -carbethoxy- $\gamma$ -cyanobutyrate; b.p. 96-100 (0.1 mm) [lit.<sup>132</sup> b.p. 175-18- (25 mm), b.p.<sup>133</sup> 104-110 (0.6 mm)]; infrared absorption, ( $\text{CCl}_4$ ) at  $2240 \text{ cm}^{-1}$  (nitrile  $-\text{C}\equiv\text{N}$ ) and  $1735 \text{ cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  4.23 (4H quartet,  $-\text{CH}_2-\text{Me}$ ), at  $\delta$  3.46 (1H, Triplet-C-H) at  $\delta$  2.7-2.4 (4H, multiplet  $\text{CN}-\text{CH}_2-\text{CH}_2-$ ), and at  $\delta$  1.27 (6H, triplet,  $\text{CH}_3-$ ); and mass spectrum  $m/e$  213 ( $\text{M}^+$ ) and abundant fragments 168, 133, 115, 101, 96, 88, 54, 43, and 29.

II. Into a 25-ml. Volumetric flask 8.81 g. (0.055 moles, 2.2 M) of diethyl malonate was directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 25-ml. volumetric flask 2.65 g. (0.05 moles, 2.0 M) of acrylonitrile was directly weighed and diluted to the mark with acetonitrile. The diethyl malonate solution was added to a three necked 100-ml. round-bottom flask equipped with a magnetic stirring bar, ground-glass stopper, rubber septum, and thermometer. To the diethyl malonate solution 1.30 g. (0.0049

moles, 0.098 M) of 18-crown-6 was added and allowed to stir for five minutes. Then 3.20 g. (0.055 moles) of dry, hot potassium fluoride was added to the diethyl malonate solution and allowed to stir five minutes. The acrylonitrile solution was slowly added by syringe over a thirty-five-minute period to allow the solution to heat slowly not exceeding 40° C. The reaction mixture was stirred until the temperature dropped to 25° C and remained stable. This required a four-hour period. The reaction mixture was then poured into 100-ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer removed. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator. This left a light yellow oil which did not solidify after three days in a freezer. The material after distillation yielded 3.5 g. (0.022 moles), b.p. 40° C (0.1 mm), of diethyl malonate. The pot material was removed and solidified. The solid material after sublimation in vacuo yielded 5.18 g. (73%) of  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile; m.p. 54-56° C [lit.<sup>130,131</sup> m.p. 61° C].

#### Ethyl Acrylate and Ethyl Cyanoacetate Condensation

I. Into a 25-ml. volumetric flask 6.22 g. (0.055 moles, 2.2 M) ethyl cyanoacetate was directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 25-ml. volumetric flask 10.0 g. (0.1 moles, 4.0 M) ethyl acry-



late was directly weighed and diluted to the mark with acetonitrile. The ethyl cyanoacetate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer. To the ethyl cyanoacetate solution 1.30 g. (0.0049 moles, 0.098 M) of 18-crown-6 was added and allowed to stir five minutes. Then 2.90 g. (0.05 moles) of dry, hot potassium fluoride was added to the ethyl cyanoacetate solution and allowed to stir for five minutes. The ethyl acrylate solution was slowly added by syringe over a five-minute period. The reaction mixture heated rapidly to 40° C during this time. The flask was immersed in an ice-water bath, cooled to a temperature of 30° C, and removed. The temperature increased slowly but stabilized below 40° C and slowly dropped to 26° C over the next hour. The reaction was monitored by glpc (3% SE 30, 5' x 1/4", 58° C) for disappearance of ethyl acrylate decreased rapidly during the first ten minutes of the reaction and remained constant over the next twelve hours. After 12.8 hours of reaction time, the reaction mixture was poured into 100-ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 11.8 g. (75%) of diethyl  $\gamma$ -

carbethoxy- $\gamma$ -cyanopimelate; b.p.  $156^{\circ}$  (0.15 mm) [lit.<sup>144</sup> b.p.  $228^{\circ}$  (20 mm)]; infrared absorption ( $\text{CCl}_4$ )  $1740\text{ cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  4.21 (6 H, quartet,  $-\text{CH}_2-\text{Me}$ ), at  $\delta$  2.7-1.9 (8 H, multiplet,  $-\text{CH}_2-\text{CH}_2-\text{COOEt}$ ), and at  $\delta$  1.30 (9 H, triplet,  $-\text{CH}_3$ ); mass spectrum,  $m/e$  313 ( $\text{M}^+$ ) and abundant fragments  $m/e$  268, 222, 213, 194, 167, 108, 55, and 28;  $^{13}\text{C}$ MR peaks ( $\text{CDCl}_3$ , internal TMS) at -117.944 (1 C, nitrile,  $-\text{C}=\text{N}$ ).

Similarly, the same reaction was conducted in the absence of 18-crown-6. The decrease in ethyl acrylate was followed by glpc (3% SE 30, 5' x 1/4",  $58^{\circ}\text{C}$ ) over a 12.8 hour period. After 2.9 hours of reaction time the ethyl acrylate had decreased by 90% compared to 97% at 12.8 hours. After the passage of the 12.8 hours of reaction time, the reaction mixture after work up, as above, yielded 10.6 g. (67%) of diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate; b.p.  $148-149^{\circ}\text{C}$  (0.08 mm).

II. Into a 50-ml. volumetric flask 10.0 g. (0.0084 moles, 1.77 M) of ethyl cyanoacetate and 2.30 g. (0.0089 moles, 0.179 M) of 18-crown-6 was directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 50-ml. volumetric flask 17.7 g. (0.177 moles, 3.54 M) of ethyl acrylate was directly weighed and diluted to the mark with acetonitrile. The ethyl cyanoacetate solution was added to a three necked 250-ml. round bottom flask equipped with magnetic stirring bar, ground glass stopper, rubber septem, and thermometer. To the ethyl cyanoacetate solution 10.0 g. (0.172 moles) of

hot, dry potassium fluoride was added and allowed to stir for 15 minutes. The ethyl acrylate solution was slowly added by syringe over a ten-minute period. The reaction mixture heated rapidly to  $43^{\circ}$  C during this period. The flask was immersed in an ice-water bath, cooled to a temperature of  $20^{\circ}$  C, and removed. The reaction mixture warmed again to  $35^{\circ}$  C, but slowly dropped toward room temperature. After one hour and fifteen minutes the reaction mixture was filtered to remove the potassium fluoride. A sample was removed and examined by NMR for vinyl proton resonance corresponding to ethyl acrylate. No vinyl proton resonance was found and the sample was returned to the reaction mixture. The reaction mixture was poured into a separatory funnel and 100 ml. of water added. The mixture was shaken vigorously and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 17.6 g. (63.4%) of diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate; b.p.  $141-143^{\circ}$  C (0.05 mm).

Similarly, the same reaction was conducted in the absence of 18-crown-6. A slow rise in temperature was noted reaching  $40^{\circ}$  C in thirty minutes. The flask was immersed in an ice-water bath, cooled to a temperature of  $20^{\circ}$  C, and removed. The reaction mixture warmed to room temperature. After 1.5 hours of reaction time, the mixture was filtered re-

moving the potassium fluoride. A sample was removed and examined by NMR for vinyl proton resonance corresponding to ethyl acrylate. Vinyl proton resonance was found. The sample was returned to the reaction mixture. The reaction mixture after the work up, as above, yielded 9.91 g. (36%) of diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate; b.p. 138-140<sup>0</sup> C (0.05 mm).

III. Into a 25-ml. volumetric flask 6.22 g. (0.055 moles, 2.2 M) ethyl cyanoacetate was directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 25-ml. volumetric flask 5.0 g. (0.05 moles, 2 M) of ethyl acrylate was directly weighed and diluted to the mark with acetonitrile. The ethyl cyanoacetate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer. To the ethyl cyanoacetate solution 1.30 g. (0.0049 moles, 0.098 M) of 18-crown-6 was added and allowed to stir for five minutes. Then 2.9 g. (0.05 moles) of dry, hot potassium fluoride was added and allowed to stir for five minutes. The ethyl acrylate solution was slowly added by syringe over a twenty-minute period with the reaction not heating to 35<sup>0</sup> C. The reaction was monitored by glpc (3% SE 30. 5' x 1/4", 58<sup>0</sup> C) for disappearance of ethyl acrylate. No change in the peak size of the ethyl acrylate was noted from the initial injection (reaction time 25 minutes) over the next three hours. The reaction mixture was stirred an additional nine hours, at which time, the reaction mixture was poured into 100 ml. of

water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 2.4 g. (0.021 moles) of recovered, ethyl cyanoacetate b.p.  $40^\circ \text{C}$  (0.1 mm) and 5.8 g. (64% based on ethyl cyanoacetate reacted) of diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate b.p.  $148^\circ \text{C}$  (0.08 mm).

#### Ethyl Acrylate and Diethyl Malonate Condensation

I. Into a 25-ml. volumetric flask 8.81 g. (0.055 moles, 2.2 M) diethyl malonate and 1.30 g. (0.0049 moles, 0.19 M) of 18-crown-6 were directly weighed and diluted to the mark with the addition of acetonitrile. Into a second 25-ml. volumetric flask 10.0 g. (0.1 moles, 4 M) of ethyl acrylate was directly weighed and diluted to the mark with acetonitrile. The diethyl malonate, 18-crown-6 solution was added to a three necked 100-ml. round bottom flask equipped with a stirring bar, ground glass stopper, rubber septum, and thermometer. Then 3.2 g. (0.055 moles) of dry, hot potassium fluoride was added to the diethyl malonate solution and allowed to stir for five minutes. The ethyl acrylate solution was added by syringe over a six-minute period. The reaction mixture heated slowly over a thirty-minute period to  $40^\circ \text{C}$ , afterwards slowly cooling to room temperature in forty-five minutes. The reaction

was monitored by glpc (3% SE 30, 5' x 1/4", 58° C) for disappearance of ethyl acrylate. A steady decline was noted in ethyl acrylate concentration for 2.9 hours of reaction time, whereby, no further decrease in ethyl acrylate was noted. After twenty-one hours of reaction time, the reaction mixture was poured into 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 10.5 g. (58%) of diethyl  $\gamma$ ,  $\gamma$ -dicarbethoxypimelate; b.p. 142-145° C (0.05 mm) [lit. <sup>117</sup> b.p. 217-219° C/20 mm, b.p. 215° C (12 mm)<sup>135</sup>]; infrared absorption ( $\text{CCl}_4$ ) 1735  $\text{cm}^{-1}$  (ester C=O); NMR peaks ( $\text{CDCl}_3$ , internal TMS)  $\delta$  4.2 (8 H, quartet,  $-\text{CH}_2\text{Me}$ ), at  $\delta$  2.24 (8 H, singlet,  $-\text{CH}_2-\text{CH}_2-\text{COOEt}$ ) and at  $\delta$  1.2 (12 H, triplet,  $\text{CH}_3-$ ); mass spectrum of abundant fragments, m/e 315, 260, 241, 214, 195, 186, 153, 140, 127, 55, and 29.

Similarly, the same reaction was conducted in the absence of 18-crown-6. No decrease was noted in the ethyl acrylate concentration over a three-hour monitoring period. The reaction mixture was allowed to stir over a four-day period. After the passage of this time, the reaction after the work up, as above, yielded 5.29 g. (0.022 moles) of recovered diethyl malonate 32° C (0.08 mm), and 3.12 g (36% based on re-

covered diethyl malonate) of diethyl  $\alpha$ -carbethoxy glutarate; b.p.  $90^{\circ}$  C (0.05 mm) [lit.<sup>135</sup> b.p. 157-158 (12 mm)]; infrared absorption ( $\text{CCl}_4$ )  $1735\text{ cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  4.19 (6 H quartet,  $\text{CH}_2\text{Me}$ ), at  $\delta$  3.46 (1 H, triplet,  $-\text{C}-\text{H}$ ), and  $\delta$  2.6-2.0 (4 H, multiplet,  $-\text{CH}_2-\text{CH}_2-\text{COOEt}$ ), and at  $\delta$  1.22 (9 H, triplet,  $\text{CH}_3-$ ); mass spectrum,  $m/e$  260 ( $\text{M}^+$ ) and abundant fragments  $m/e$  215, 169, 133, 115, 43, and 29.

II. Into a 25-ml. volumetric flask 8.81 g. (0.055 moles, 2.2 M) of diethyl malonate was directly weighed and diluted to the mark with acetonitrile. Into a second 25-ml. volumetric flask 5.0 g. (0.05 moles, 2 M) of ethyl acrylate was directly weighed and diluted to the mark with acetonitrile. The diethyl malonate solution was added to a three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer. To the diethyl malonate solution 1.30 g. (0.0049 moles, 0.0098 M) 18-crown-6 was added and allowed to stir for five minutes. Then 3.2 g. (0.055 moles) of dry, hot potassium fluoride was added and allowed to stir for five minutes. The ethyl acrylate solution was slowly added by syringe over a five-minute period. The solution was allowed to stir for three hours. Then the reaction mixture was poured into 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The

organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 7.23 g. (62%) of diethyl  $\alpha$ -carbethoxyglutarate b.p.  $97.5^\circ \text{C}$  (0.08 mm) and 2.91 g. of pot material. The pot material was redistilled and yielded 1.32 g. (8%) of diethyl  $\gamma, \gamma$ -dicarbethoxypimelate b.p.  $146^\circ \text{C}$  (0.08 mm).

#### Ethyl Acrylate and Cyclohexanone Condensation

A three necked 100 ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, rubber septum, and thermometer was charged with 10.11 g (0.103 moles) of cyclohexanone and 2.70 g. (0.0102 moles) of 18-crown-6 in 30 ml. of acetonitrile. To this solution was added 12 g. (0.21 moles) of dry, hot potassium fluoride and allowed to stir for one hour. Then, 10.3 g. (0.103 moles) of ethyl acrylate was slowly added by syringe over a 45-minute period. No temperature increase was noted at all. After two days time, no definitive change in the reaction mixture was noted. Therefore, a reflux condenser equipped with a drying tube of calcium chloride was added to the reaction vessel. The material was refluxed for five days over which time the reaction mixture turned a dark brown. Refluxing was stopped and the mixture was poured into 150 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 125 ml. of diethyl ether. The organic layer and ether ex-



tracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 2.1 g. (0.024 moles) of cyclohexanone and 1.20 g. (8%) of ethyl 2-oxocyclohexanepropionate; b.p.  $104-109^\circ \text{C}$  (0.3 mm) lit.<sup>136</sup> b.p.  $96-100^\circ \text{C}$  (0.13 mm) ; infrared absorptions ( $\text{CCl}_4$ )  $1715 \text{ cm}^{-1}$  (ketone  $\text{C}=\text{O}$ ) and  $1735 \text{ cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks (internal, TMS) at  $\delta$  3.95 (2 H, quartet,  $-\text{CH}_2-\text{Me}$ ) at  $\delta$  2.5-1.2 (13 H, multiplet) and at  $\delta$  1.05 (3 H, triplet,  $-\text{CH}_3$ ); mass spectra,  $m/e$  198 ( $\text{M}^+$ ). The pot material was redistilled and yielded 1.99 g. (9%) diethyl 2-oxocyclohexanebis (dipropionate); b.p.  $155^\circ \text{C}$  (0.15 mm) [lit.<sup>137</sup> b.p.  $145^\circ \text{C}$  (0.05 mm)]; infrared absorption ( $\text{CCl}_4$ )  $1708 \text{ cm}^{-1}$  (ketone  $\text{C}=\text{O}$ ) and  $1728 \text{ cm}^{-1}$  (ester  $\text{C}=\text{O}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  4.14 (4 H, quartet,  $\text{CH}_2-\text{Me}$ ), at  $\delta$  2.7-1.5 (16 H, multiplet) and at  $\delta$  1.23 (6 H, triplet,  $\text{CH}_3-$ ); mass spectra,  $m/e$  298 ( $\text{M}^+$ ) and abundant fragments are 253, 207, 198, 189, 165, 152, 123, 67, 55, and 29. No further attempts were made to improve yields. A large quantity of tar remained in the distillation flask.

### Knoevenagel Condensations

#### Malononitrile and Benzaldehyde Condensation

Into a 50-ml. volumetric flask 10.6 g. (0.1 moles, 2 M) of benzaldehyde, 6.61 g. (0.1 moles, 2 M) of malononitrile, and 2.64 g. (0.01 moles, 0.2 M) of 18-crown-6 were directly weighed and sealed with a rubber septum. Then dry benzene

was added to the volumetric by canulla to the mark and the solution shaken until homogeneous. A three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, thermometer, rubber septum, and condenser with a drying tube of calcium chloride was charged with the benzene solution. Then 1.55 g. (0.026 moles) of dry, hot potassium fluoride was added to the benzene solution and stirred vigorously. The solution immediately turned a deep red color accompanied by a rise in temperature to approximately  $68^{\circ}$  C. The formation of a second phase which was water was also noted. The reaction was followed by glpc (3% SEC-30, 5' x 1/4",  $100^{\circ}$  C) for the disappearance of benzaldehyde. After ten minutes of reaction time, a substantial decrease in benzaldehyde was noted (comparing the peak area of benzaldehyde at a given reaction time to the initial peak area of benzaldehyde before potassium fluoride was added). After one hour reaction time, the reaction mixture was poured into 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give a red solid. The solid after sublimation in vacuo yielded 11.9 g. (77%) of benzylidenemalononitrile; m.p.  $81-83^{\circ}$  C [lit.<sup>138</sup> m.p.  $83.5-84.0^{\circ}$  C]; infrared spectrum absorption (KBr)  $2225\text{ cm}^{-1}$  (nitrile,  $\text{C}\equiv\text{N}$ ); NMR peaks ( $\text{CDCl}_3$ , internal

TMS) at  $\delta$  8.2-7.2 (6 H, multiplet, phenyl--CH=); mass spectrum,  $m/e$ , 154 ( $M^+$ ) and abundant fragments 127, 103, 76, 51, and 32. Approximately 1.5 g. of solid material was left in the sublimation apparatus as a gum which could not be characterized.

Similarly, the same reaction was conducted in the absence of 18-crown-6. The decrease in benzaldehyde was followed by glpc (3% SEC-30, 5' x 1/4", 100° C) over a 16.8 hour period whereby, the benzaldehyde had slowly decreased. The reaction mixture stirred for nine days and after the work up, as above, yielded 13.1 g. (84%) benzylidenemalononitrile, m.p. 81-83° C.

#### Malononitrile and Cyclohexanone Condensation

Into a 50-ml. volumetric flask 9.8 g. (0.1 moles, 2 M) of cyclohexanone, 6.61 g. (0.1 moles, 2 M) of malononitrile, and 2.64 g. (0.01 moles, 0.2 M) of 18-crown-6 were directly weighed and sealed with a rubber septum. Then dry benzene was added to the volumetric by cannula to the mark and the solution shaken until homogeneous. A three necked 100-ml. round-bottom flask equipped with a magnetic stirring bar, thermometer, rubber septum, and condenser with a drying tube of calcium chloride was charged with the benzene solution. Then 1.55 g. (0.026 moles) of dry, hot potassium fluoride was added to the benzene solution and stirred vigorously. The solution immediately changed color to a dark yellow, accompanied by a rise in temperature to approximately 60° C. The formation of a second phase, which was water, was also noted. The reaction was followed by glpc (3% SEC-30, 5' x 1/4", 89° C) for the

disappearance of cyclohexanone. After ten minutes, a large decrease in the cyclohexanone was noted (comparing the peak area of cyclohexanone at a given reaction time to the initial peak area of cyclohexanone before potassium fluoride was added). After one hour of reaction time, the reaction mixture was filtered to remove a yellow crystalline material, m.p. 124.5-129° C, which was shown to be a novel 1:2 crown-malononitrile complex (to be discussed later in further detail). The reaction mixture was then poured into 100-ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 10.5 g. (72%) of cyclohexylidenemalononitrile; b.p. 69-70° C (0.5 mm) [lit.<sup>139</sup> b.p. 137-138° C (10 mm)]; infrared absorption (neat) 2235  $\text{cm}^{-1}$  (nitrile,  $\text{C}\equiv\text{N}$ ) and 1599  $\text{cm}^{-1}$  (double bond,  $\text{C}=\text{C}$ ): NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  2.8-2.4 (4 H, multiplet) and  $\delta$  2.1-1.4 (6 H, multiplet); mass spectra, m/e 146 ( $\text{M}^+$ ) and abundant fragments 131, 118, 105, 92, 81, 69, 55, and 41.

Similarly, the same reaction was conducted in the absence of 18-crown-6. The decrease in cyclohexanone was followed by glpc (3% SEC-30, 5' x 1/4, 89° C) over a one hour period, whereby the cyclohexanone had slowly decreased steadily.

The reaction mixture was stopped after one hour and the work up, as above, yielded 9.9 g. (68%) of cyclohexylidenemalononitrile, b.p. 67-68° C (0.5 mm).

#### Ethylcyanoacetate and Benzaldehyde Condensation

Into a 50-ml. volumetric flask 10.6 g. (0.1 moles, 2 M) of benzaldehyde, 11.3 g. (0.1 moles, 2 M) of ethyl cyanoacetate, and 2.64 g. (0.01 moles, 0.2 M) of 18-crown-6 were directly weighed and sealed with a rubber septum. Then dry benzene was added to the volumetric by cannula to the mark and the solution shaken until homogeneous. A three-necked 100-ml. round-bottom flask equipped with a magnet stirring bar, thermometer, and ground-glass stopper was charged with the benzene solution. Then 1.55 g. (0.026 moles) of dry, hot potassium fluoride was added to the benzene solution and stirred vigorously. The solution immediately turned a deep red color accompanied by a rise in temperature to approximately 60° C. The reaction was followed by glpc (3% SEC-30, 5' x 1/4", 100° C) for the disappearance of benzaldehyde. After twelve minutes only a trace of benzaldehyde was present. After six hours of reaction, the reaction mixture was poured into 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give a solid. The solid after sublima-

tion in vacuo yielded 16.3 g. (81%) of ethyl benzylidene-cyanoacetate; m.p. 48-49° C [lit.<sup>30</sup> m.p. 50-52° C]; infrared absorptions (KBr) 2225 cm<sup>-1</sup> (nitrile, C≡N), 1725 cm<sup>-1</sup> (ester, C=O), and 1615 cm<sup>-1</sup> (double bond, C=C); NMR peaks (CDCl<sub>3</sub>, internal TMS) at δ 8.28 (1 H, singlet, H-C=C), δ 8.1-7.3 (5 H, multiplet, phenyl-), δ 4.4 (2 H, quartet, -CH<sub>2</sub>Me), and δ 1.33 (3 H, triplet, CH<sub>3</sub>-); mass spectrum, m/e 201 (M<sup>+</sup>) and abundant fragments at 200, 172, 156, 128, 102, 77, and 51.

Similarly, the same reaction was conducted in the absence of 18-crown-6. The decrease in benzaldehyde was followed by glpc (3% SEC-30, 5' x 1/4", 100° C) over a six-day period, whereby the benzaldehyde had slowly decreased. After six days the reaction mixture was worked up, as above, and yielded 9.18 g. (46%) of ethyl benzylidenecyanoacetate, m.p. 48-49° C.

#### Diethyl Malonate and Benzaldehyde Condensation

Into a 50-ml. volumetric flask 10.6 g. (0.1 moles, 2 M) of benzaldehyde, 16.0 g. (0.1 moles, 2 M) of diethyl malonate, and 2.64 g. (0.01 moles, 0.2M) of 18-crown-6 were directly weighed and sealed with a rubber septum. Then dry benzene was added to the volumetric by canulla to the mark and the solution shaken until homogeneous. A three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, thermometer, ground glass stopper, and Dean-Stark trap was charged with the benzene solution. Then 1.55 g. (0.026 moles) of dry, hot potassium fluoride was added to the benzene solution and stirred vigorously. The solution was heated to re-

fluxing with the internal temperature reaching  $92^{\circ}\text{C}$ . After twelve hours of reaction time, water was noted in the Dean-Stark trap. After three days, the solution had turned black and 0.7 m. of water was in the Dean-Stark trap. The reaction was then stopped and poured into 100 ml. of water. The aqueous mixutre was poured into a separatory funnel and the organic layer separated. The aqueous phase was extracted twice with 300 ml. of diethyl ether. The organic layer and ether extracts were combined, dired over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 8.1 g. (33%) of ethyl benzalmalonate; b.p.  $120-124^{\circ}\text{C}$  (0.11 mm) [lit.<sup>140</sup> b.p.  $140-142^{\circ}\text{C}$  (4 mm)]; infrared absorption ( $\text{CCl}_4$ )  $1730\text{ cm}^{-1}$  (ester,  $\text{C=O}$ ), and  $1630\text{ cm}^{-1}$  (double bond,  $\text{C=C}$ ); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  7.74 (1 H, singlet,  $\text{H-C=C-}$ ), at  $\delta$  7.6-7.2 (5 H, multiplet, phenyl), at  $\delta$  4.6-4.0 (4 H, octet,  $-\text{CH}_2-\text{Me}$ ), and  $\delta$  1.5-1.1 (6 H, sextet,  $-\text{CH}_3$ ): mass spectrum, m/e 248 ( $\text{M}^+$ ), and abundant fragments 203, 174, 158, 131, 130, 102, 77, and 29.

Similarly, the same reaction was conducted in the absence of 18-crown-6. No water was found in the Dean-Stark trap and the work up, as above, yielded only starting material, diethyl malonate.

### Alkylations

#### Diethyl Malonate with Benzyl Bromide

Into a 50-ml. volumetric flask 9.4 g. (0.059 moles,

1.18 M) of diethyl malonate, 10.0 g. (0.59 moles, 1.18 M) of benzyl bromide and 1.55 g. (0.0058 moles, 0.12 M) of 18-crown-6 were directly weighed and diluted to the mark with acetonitrile. The acetonitrile solution was thoroughly shaken until homogeneous. A three necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, and rubber septum was charged with the acetonitrile solution. Then 13.5 g. (0.23 moles) of dry, hot potassium fluoride was added to the acetonitrile solution and stirred vigorously. The reaction was monitored by glpc (3% SE 30, 5' x 1/4", 100° C) for the disappearance of benzyl bromide. After 41 hours of reaction time, no benzyl bromide could be detected. The reaction mixture was filtered to remove the potassium fluoride and then poured into 100 ml. of water. The solid material was washed with diethyl ether. The aqueous mixture was poured into a separatory funnel and extracted twice with 300 ml. of diethyl ether. The ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo yielded 1.1 g. (0.007 moles) of recovered diethyl malonate 40° C (0.11 mm) and 9.14 g. (63% based on recovered diethyl malonate) of diethyl benzylmalonate; b.p. 100-105° C (0.11 mm) [lit.<sup>141</sup> b.p. 150-160° C (7 mm)]; infrared absorption ( $\text{CCl}_4$ ) 1735  $\text{cm}^{-1}$  (ester C=O); NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  7.2 (5 H, singlet, ArH), at  $\delta$  4.1 (4 H, quartet,



-CH<sub>2</sub>-Me), at  $\delta$  3.68 (1 H, quartet, C-H), at  $\delta$  3.20 (2 H, doublet, Ar-CH<sub>2</sub>-), and at  $\delta$  1.1 (6 H, triplet, CH<sub>3</sub>-): mass spectrum, m/e 250 (M<sup>+</sup>) and abundant fragments 205, 176, 159, 148, 131, 103, 91, 77, 51, and 29. There was 2.72 g. of pot material remaining which was redistilled to give 1.34 g. (12.1% based on recovered diethyl malonate) of diethyl dibenzylmalonate; b.p. 143-148° C (0.24 m) [lit.<sup>142</sup> 234-5 (23 mm)]; infrared absorptions (CCl<sub>4</sub>) 1735 cm<sup>-1</sup> (ester, C=O) and 1601 cm<sup>-1</sup> (double bond, phenyl); NMR peaks (CDCl<sub>3</sub>, internal TMS) at  $\delta$  7.2 (10 H, singlet, ArH), at  $\delta$  4.1 (4 H, quartet, -CH<sub>2</sub>-Me), at  $\delta$  3.24 (4 H, singlet, -CH<sub>2</sub>-), and at  $\delta$  1.1 (6 H, triplet, CH<sub>3</sub>-); mass spectrum, m/e 340 (M<sup>+</sup>) and abundant fragments 295, 249, 203, 192, 115, 91, 65, and 29.

Similarly, the same reaction was conducted in the absence of 18-crown-6. No change in benzyl bromide was noted by glpc (3% SE-30, 5' x 1/4", 100° C) and the work up, as above, yielded only the starting material diethyl malonate.

#### Diethyl Malonate with Benzyl Chloride

Into a 50-ml. volumetric flask 9.4 g. (0.059 moles, 1.18 M) of diethyl malonate, 7.4 g. (0.059 moles, 1.18 M) of benzyl chloride and 1.58 g. (0.006 moles, 0.12 M) of 18-crown-6 were directly weighed and diluted to the mark with acetonitrile. The acetonitrile solution was thoroughly shaken until homogeneous. A three-necked 100-ml. round bottom flask equipped with a magnetic stirring bar, ground glass stopper, and rubber septum was charged with the acetonitrile solution. Then

13.5 g. (0.23 moles) of dry, hot potassium fluoride was added to the acetonitrile solution and stirred vigorously. The reaction was monitored by glpc (3% SE-30, 5' x 1/4", 100° C) for the disappearance of benzyl chloride. After 186 hours of reaction, only a trace of benzyl chloride could be detected. The reaction mixture was filtered to remove the potassium fluoride and then poured into 100 ml. of water. The solid material was washed with diethyl ether. The aqueous mixture was poured into a separatory funnel and extracted twice with 300 ml. of diethyl ether. The ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil upon distillation gave 1.25 g. (0.008 moles) of recovered diethyl malonate 40° C (0.1 mm) and 8.1 g. (56% based on recovered diethyl malonate) of diethyl benzylmalonate, b.p. 105-110 (0.15 mm). There was also isolated 1.00 g. (10% based on recovered diethyl malonate) of diethyl dibenzylmalonate.

Similarly, the same reaction was conducted in the absence of 18-crown-6. No change in benzyl chloride was noted by glpc (3% SE-30, 5' x 1/4", 100° C) and the work up, as above, yielded only the starting material diethyl malonate.

#### Diethyl Malonate with Methyl Iodide

Into a 25-ml. volumetric flask 10.0 g. (0.0624 moles, 2.50 M) of diethyl malonate, 9.2 g. (0.0648 moles, 2.59 M) of methyl iodide, and 1.7 g. (0.0064 moles, 0.26 M) of 18-crown-6 were directly weighed and diluted to the mark with acetonitrile.

The acetonitrile solution was thoroughly shaken until homogeneous. The acetonitrile solution was poured into a 50-ml. round bottom flask, 10.9 g. (0.188 moles) of dry, hot potassium fluoride was added, and the round bottom flask was sealed with a rubber septum quickly. The reaction mixture was agitated by means of a wrist-action shaker and monitored by glpc (3% SE-30, 5' x 1/4" , 90° C) for disappearance of diethyl malonate. After 58 days, the reaction mixture showed that the diethyl malonate had decreased and the reaction was stopped. The reaction mixture was poured into a 100 ml. of water and stirred. The aqueous mixture was poured into a separatory funnel and extracted twice with 300 ml. of diethyl ether. The ether extracts were combined, dried over  $\text{MgSO}_4$ , filtered under a vacuum, and the ether removed on a rotary evaporator to give an oil. The oil after distillation in vacuo at 41° C (0.1 mm) gave 6.13 g. of a mixture of diethyl malonate and diethyl methylmalonate. Glpc (bromocyclohexane internal standard, 3% SE-30, 5' x 1/4", 90° C) showed the mixture to consist of 13% diethyl malonate (0.797 g.) and 5.33 g. (53.4% based on recovered diethyl malonate) diethyl methylmalonate. Actual samples of pure material were used to identify the above compounds.

Similarly, the same reaction was conducted in the absence of 18-crown-6. A slower reaction was noted and the work up, as above, yielded 4.21 g. of a mixture of diethyl malonate and diethyl methylmalonate. Glpc (bromocyclohexane internal

standard, 3% SE-30, 5' x 1/4", 90° C) showed the mixture to consist of 46% diethyl malonate (1.95 g.) and 2.26 g. (26% based on recovered diethyl malonate) of diethyl methylmalonate.

### 18-Crown-6 Complexes

#### Cyanogen Bromide/18-crown-6 Complex

I. To a vial containing approximately seven ml. of dry diethyl ether was added 18-crown-6 until the solubilization became difficult. Then solid crystals of cyanogen bromide (Eastman Kodak) were added to the ether solution and solubilized by crushing the crystals with a spatula until all the solid dissolved. This procedure was followed until fine white crystals began to precipitate from the solution. The solution was then filtered and the solution collected. The solution was placed in a vial and sealed under N<sub>2</sub>. After a week a large monoclinic crystal formed approximately 5mm. by 3mm. The complex had a melting point at 64.5-68° C; infrared absorptions (nujol) 2160 cm<sup>-1</sup> (nitrile, C≡N) and 1100 cm<sup>-1</sup> (ether, C-O); NMR peaks (CDCl<sub>3</sub>, internal TMS) δ 3.7 (crown ether); crystal density,<sup>143</sup> calc. 1.529 g/ml, found 1.526 g/ml.

II. To a vial containing five ml. of carbon tetrachloride was added 18-crown-6 and the mixture was heated to dissolve 18-crown-6. This procedure was repeated until no more 18-crown-6 could be solubilized. Then solid cyanogen bromide (Eastman) was added to the hot solution and dissolved by

crushing the solid with a spatula until the solution turned milky in color. Then the solution was heated again and allowed to cool slowly to room temperature. Nice prism crystals precipitated from the solution. The crystals were filtered from the carbon tetrachloride under  $N_2$  in a glove bag and sealed in a vial. The density of the crystals was measured in carbon tetrachloride and benzene. The value obtained was 1.514 g/ml and 1.517 g/ml compared to 1.529 g/ml, calculated value. The m.p. of these crystals agreed with the above m.p. of the complex.

Anal. Calcd. for  $C_{12}H_{24}O_6 (CNBr)_2$ : C, 35.31; H, 5.08; N, 5.89; Br, 33.57. Found; C, 38.45; H, 5.81; N, 5.02; Br, 28.39.

#### Malonitrile/18-Crown-6 Complex

To eight ml. of dry benzene was added 2.0 g. (0.0076 moles) 18-crown-6 and 1.5 g. (0.023 moles) malonitrile. The solution was heated until solubilization was effected and then allowed to cool to room temperature. A white crystalline solid precipitated and was collected by filtration. The material was recrystallized from dry benzene and yielded uniform needle crystals of malonitrile/18-crown-6 complex; m.p. 127-129° C; NMR peaks ( $CD_3CN$ , internal TMS) at  $\delta$  3.9 (4 H, singlet, malononitrile) and at  $\delta$  3.7 (24 H, singlet, crown); infrared absorption (nujol mull) 2242  $cm^{-1}$  (nitrile,  $C\equiv N$ );  $^{13}C$  MR (acetone- $d_6$ , internal TMS standard) at  $\delta$  -70.742 (methylene,  $-CH_2-O$ );  $^{13}C$  NMR (acetonitrile- $d_3$ , internal TMS standard) at

$\delta$  -112.790 (nitrile,  $-\text{C}\equiv\text{N}$ ), at  $\delta$  -70.985 (methylene  $-\text{CH}_2-\text{O}$ ).

Anal. Calculated for  $\text{C}_{12}\text{H}_{14}\text{O}_6 (\text{C}_3\text{H}_2\text{N}_2)_2$ : C, 54.43; H, 7.12; N, 14.14; O, 24.21. Found; C, 54.47; H, 7.14; N, 14.16; O, 24.23.

#### Succinonitrile/18-Crown-6 Complex

To eight ml. of dry benzene was added 0.202 g. succinonitrile (0.0025 moles) and one gram of 18-crown-6 (0.0038 moles). The solution was heated until solubilization was effected and then allowed to cool to room temperature. Then the solution was cooled in an ice-water bath to effect precipitation. A white, crystalline solid precipitated and was collected by filtration. The material was recrystallized from carbon tetrachloride to give needle crystals of succinonitrile/18-crown-6 complex; m.p.  $83-84^\circ\text{C}$ ; NMR peaks ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  3.7 (24 H, singlet, crown) and  $\delta$  2.9 (8 H, singlet, succinonitrile); infrared absorption (nujol mull)  $2221\text{ cm}^{-1}$  (nitrile,  $\text{C}\equiv\text{N}$ );  $\text{C}^{13}$  MR ( $\text{CDCl}_3$ , internal TMS) at  $\delta$  -118.129 (nitrile,  $\text{C}\equiv\text{N}$ ) and at  $\delta$  -70.713 (methylene,  $-\text{CH}_2-\text{O}$ ).

Anal. Calculated for  $\text{C}_{12}\text{H}_{14}\text{O}_6 (\text{C}_4\text{H}_4\text{N}_2)_2$ : C, 56.55; H, 7.60; N, 22.62; O, 13.20. Found: C, 57.06; H, 7.68; N, 21.98; O, 13.28.

## CHAPTER III

## RESULTS AND DISCUSSIONS

As noted earlier, the main use of potassium fluoride in organic chemistry has been as a fluorinating agent, although reports indicate the ability of fluoride ions to act as a base.<sup>22-45</sup> The major problem in using potassium fluoride in either system has been the insolubility of the material in organic solvents. Liotta and Harris<sup>122,123</sup> have had remarkable success in solubilizing potassium fluoride in polar and nonpolar, aprotic solvents (acetonitrile and benzene) with the aid of 18-crown-6; the resulting reagent was effective in fluorination. The capabilities of the "naked" fluoride ion to behave as a base was investigated in the present work. Selected Michael, Knoevenagel, and alkylation reactions were conducted at room temperature with the following general conclusion: the reactions using "naked" fluoride ions required shorter reactions times and produced better, or at least equivalent, yields of products than the reactions with no 18-crown-6.

All the reactions were carried out in acetonitrile, except the Knoevenagel reactions which were carried out in benzene. These solvents were used since they are low boiling and inert to the fluoride anion. The 18-crown-6 ether was used in all cases only in catalytic quantities. Liotta and Harris<sup>122,123</sup> measured the solubilities of potassium fluoride

in these solvents. Their data are tabulated in Table 1. Assuming a linear relationship between the concentration of crown and the concentration of potassium fluoride, then the range of concentrations of potassium fluoride or fluoride ion in solution, used in the present reactions was approximately  $2 \times 10^{-3} \text{ M}$  to  $5.6 \times 10^{-3} \text{ M}$  in acetonitrile and  $8.2 \times 10^{-3} \text{ M}$  in benzene.

Table 1. Solubility of KF in Presence of 18-Crown-6 at  $25^\circ \text{C}$ <sup>144</sup>

Solvent	(18-Crown-6), M	(KF), M
Acetonitrile	0	$3 \times 10^{-4}$
	0.16	$3.5 \times 10^{-3}$
Benzene	1.01	$5.2 \times 10^{-2}$
	0.34	$1.4 \times 10^{-2}$

#### Michael Condensations

The Michael condensations were carried out using acrylonitrile and ethyl acrylate as substrates with ethyl cyanoacetate and diethyl malonate as reactants. The reactant to substrate molar ratio (referred to further as R/S ratio) was varied from one to one (1:1) to one to two (1:2). The results of the reactions are tabulated in Table 2.

Ethyl cyanoacetate reacted with each substrate acrylonitrile and ethyl acrylate, to generate the disubstituted products,  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile and diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate, respectively, in the presence and absence of 18-crown-6. However, the reaction times were de-



Table 2. Michael Condensations initiated by Potassium Fluoride in the Presence and Absence of 18-Crown-6

Product	Substrate Conc. (M)	Reactant Conc. (M)	Crown Conc. (M)	Temperature <sup>e</sup> °C	Time (hr)	% Yield isolated	
γ-carbethoxy-γ-cyanopimelonitrile	1.0	1.1	0.098	ambient	0.17	86	a
	1.0	1.1	0		4	80	a
	2.0	1.1	0.098	ambient	0.25	83	a
	2.0	1.1	0	25°	43	84	a
	2.0	1.1	0.098	ambient	0.25	90	a (dry CH <sub>3</sub> CN)
γ,γ-dicarbethoxy-pimelonitrile	1.0	1.1	0.098	ambient	4	73	b
	2.0	1.1	0.098	ambient	3.5	82	b
ethyl α-carbethoxy-γ-cyanobutyrate	2.0	1.1	0	25°	121	84	b
diethyl γ-carbethoxy-γ-cyanopimelate	1.0	1.1	0.098	ambient	3	64	c
	2.0	1.1	0.098	ambient	0.17	75	c
	2.0	1.1	0	ambient	13	67	c
diethyl α-carbethoxy-glutarate	1.0	1.1	0.098	ambient	3	62	d*
	2.0	1.1	0	25°	96	36	d
diethyl γ,γ-dicarbethoxy-pimelate	1.0	1.1	0.098	ambient	3	8	d*
	2.0	1.1	0.098	ambient	3	58	d

a : acrylonitrile as substrate with ethyl cyanoacetate as reactant

b : acrylonitrile as substrate with diethyl malonate as reactant

c : ethyl acrylate as substrate with ethyl cyanoacetate as reactant

d : ethyl acrylate as substrate with diethyl malonate as reactant

d\*: the same reaction

e : ambient refers to a temperature increase above room temperature for a period of time during the reaction with eventual return to room temperature

pendent on the substrate concentrations and the presence of 18-crown-6. Ethyl cyanoacetate in the presence of 18-crown-6 reacted with equal facility with acrylonitrile and ethyl acrylate when the R/S ratio was one to one (1:1). In the absence of 18-crown-6 the above reactions all had considerable longer reaction times. Even in dry acetonitrile with 18-crown-6 the disubstituted products,  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile, was isolated.

Aoyama<sup>37</sup> and Kanbe<sup>39</sup> reacted ethyl cyanoacetate with ethyl acrylate and acrylonitrile in ethanol with potassium fluoride as the base. In each case, the disubstituted products were obtained in low yields of 32% and 39%, respectively. The conditions for the reactions (R/S ratio 1:1) required seven hours at 40-50° C for acrylonitrile and refluxing ethanol for three and one-half hours for ethyl acrylate. However, with 18-crown-6 and acetonitrile, as solvent, the yields of the disubstituted products are better and compare favorable to other synthetic routes to these products.

Bruson<sup>129</sup> obtained  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelonitrile in a 98% crude yield from reacting acrylonitrile and ethyl cyanoacetate (R/S ratio 2:1) in dioxane with Triton B at 30-35° C. Similarly, Tenniswood<sup>128</sup> obtained diethyl  $\gamma$ -carbethoxy- $\gamma$ -cyanopimelate in an isolated 86% yield from reacting ethyl cyanoacetate with  $\beta$ -cyanoethyl toluene-p-sulphonate (R/S ratio 1:1) in ethanol with sodium at room temperature for 18 hours.

Diethyl malonate reacted with each substrate, acry-

lonitrile and ethyl cyanoacetate. With acrylonitrile in the presence of 18-crown-6, diethyl malonate yielded the disubstituted product  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile in both cases where the R/S ratios were one to one (1:1) and one to two (1:2). Yet, when no 18-crown-6 was present and the R/S ratio was one to two (1:2), only the monosubstituted product, ethyl  $\alpha$ -carbethoxy- $\gamma$ -cyanobutyrate was found. With ethyl acrylate in the presence of 18-crown-6, diethyl malonate yielded both the mono and disubstituted products depending on the R/S ratio. When the R/S ratio was one to one (1:1) the monosubstituted product, diethyl  $\alpha$ -carbethoxygluterate, was isolated as the major product with the minor product, the disubstituted product, diethyl  $\gamma$ ,  $\gamma$ -dicarbethoxypimelate. When the R/S ratio was one to two (1:2) only the disubstituted product, diethyl  $\gamma$ ,  $\gamma$ -dicarbethoxygluterate was isolated. However, if no 18-crown-6 was present and the R/S ratio was one to two (1:2) the only product isolated was diethyl  $\alpha$ -carbethoxygluterate. In each case, again, the reaction times were considerably shorter for the reactions with 18-crown-6 present than the reactions containing no 18-crown-6.

Kanbe<sup>38,39</sup> reacted diethyl malonate with ethyl acrylate and acrylonitrile in ethanol with potassium fluoride as the base. Kanbe found diethyl malonate and ethyl acrylate (R/S ratio 1:1) yielded only the monosubstituted product, diethyl  $\alpha$ -carbethoxygluterate with an isolated yield of 55% after refluxing for fourteen hours. On the other hand, Kanbe found

diethyl malonate and acrylonitrile (R/S ratio 1:2) yielded only the disubstituted product, diethyl  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile with an isolated yield of 68% and required heating for seven hours at 50-60° C. However, the use of acetonitrile in conjunction with 18-crown-6 gave equivalent yields, as the above, with less stringent conditions. In fact, these yields compare favorable to yields obtained by other synthetic routes.

Tenniswood<sup>128</sup> obtained both ethyl  $\alpha$ -carbethoxy- $\gamma$ -cyano-pimelonitrile and  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile in isolated yields of 33% and 34%, respectively from reacting diethyl malonate and  $\beta$ -cyanoethyl toluene-p-sulphonate (R/S ratio 1:1) in refluxing ethanol for eight hours with sodium. When the R/S ratio was one to two (1:2), only  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile was isolated in 80% yield. Bruson<sup>129</sup> isolated  $\gamma$ ,  $\gamma$ -dicarbethoxypimelonitrile in 82% yield from the reaction of diethyl malonate and acrylonitrile (R/S ratio 1:2) in dioxane with Triton B as the base at room temperature for three hours. Bankert<sup>146</sup> obtained diethyl  $\alpha$ -carbethoxyglutarate and diethyl  $\gamma$ ,  $\gamma$ -dicarbethoxypimelate in 21 and 18% isolated yields, respectively by reacting diethyl malonate and beta-propiolactone (R/S ratio 1:1) in ethanol at 30° with sodium.

Attempted Michael condensation of cyclohexanone with ethyl acrylate in the presence of 18-crown-6 yielded only small amounts of the mono and disubstituted products, ethyl 2-oxocyclohexanepropionate and diethyl 2-oxocyclohexanebis (dipropionate), respectively, even at reflux conditions. Such

low yields and long reaction time may be related to the inability of the fluoride ions to remove the alpha proton leading to the formation of the enolate.

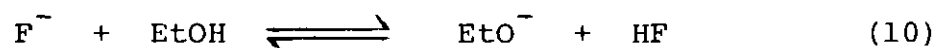
The decrease in reaction times of the Michael condensations caused by the presence of 18-crown-6 can be explained by considering two closely related processes, solubility and ion-pair association. In the presence of 18-crown-6 the solubility of potassium fluoride increases. With the increased concentration of potassium fluoride in solution, an increased concentration of "naked" fluoride ion was expected since 18-crown-6 has been shown to increase ion-pair dissociation.<sup>102-119</sup> With a reduction in solvation the "naked" fluoride ion was expected to show an increased reactivity should lead to an increase in the Michael donor carbanion concentration and a shifting of the equilibriums to the Michael adduct products with shorter reaction times which are noticed.

As noted earlier, Kanbe and Aoyama conducted Michael condensations with potassium fluoride in alcohol. The solubility of potassium fluoride in ethanol was determined by Germuth.<sup>147</sup> The data is tabulated in Table 3. As noted, the potassium fluoride is more soluble in ethanol at corresponding temperatures than in acetonitrile even with 18-crown-6 present. However, the reaction conditions used by Kanbe and Aoyama were harsher and required longer times. The longer times are undoubtedly due to solvation effects, namely hydrogen bonding,<sup>148</sup> and the decrease of the solubility of potassium fluoride at

Table 3. Solubility of KF in Anhydrous Ethanol (moles of salt per mole of ethanol)

Temperature	KF
20	0.00084 (1.4x10 <sup>-2</sup> M)
30	0.00076 (1.3x10 <sup>-2</sup> M)
40	0.00054 (9.0x10 <sup>-3</sup> M)
45	0.00039
50	0.00018
55	0.00008

higher temperatures. The equilibrium (10) between ethanol and ethoxide in the presence of potassium fluoride appears to be



negligible. Yasuda<sup>41</sup> found primary and secondary alcohols reacted easily with acrylonitrile in the presence of alkaline catalysts to form the corresponding alkoxypropionitriles. However, when ethanol was used in the presence of potassium fluoride with acrylonitrile, negligible or no ethoxypropionitrile was obtained. Kanbe and Aoyama found no alkoxy derivatives in their studies.

### Knoevenagel Condensations

The Knoevenagel condensations were carried out using benzaldehyde and in one case cyclohexanone as substrates with ethylcyanoacetate, diethyl malonate, and malononitrile as reactants. The R/S ratio was maintained at one to one (1:1). The results of these reactions are tabulated in Table 4.

Examination of Table 4 indicated the reactions carried out in the presence of 18-crown-6 have shorter times. In the case of diethyl malonate condensing with benzaldehyde, only the reaction with 18-crown-6 yielded any product even with refluxing benzene. The low yield and harsher reaction conditions for diethyl malonate may be related to slow attack on the carbonyl or a slower subsequent step, the dehydration step. The half-times ( $t_{1/2}$ ) for the condensations with malononitrile and ethyl cyanoacetate as reactants in the presence of 18-crown-6 are all of the same order, one-half minute. This value of half-time for ethyl cyanoacetate compares favorable with the half-time (1.5 min.) for the condensation of ethyl cyanoacetate and benzaldehyde with  $\epsilon$ -aminocaproic acid and acetic acid as catalyst in refluxing benzene. Potassium fluoride under similar conditions, as above, yielded half-times for the same reaction of 10 minutes with acetic acid present and 16 minutes with no acetic acid.<sup>149</sup> The expected product from the condensation of ethyl cyanoacetate and benzaldehyde was the trans product with respect to the aryl and carbethoxy groups.<sup>150</sup>

Table 4. Knoevenagel Condensations initiated by Potassium Fluoride in the Presence and Absence of 18-Crown-6

Product	Substrate Conc. (M)	Reactant Conc. (M)	Crown Conc. (M)	Temperature °C	Time (hr)	$t_{1/2}^*$ (min.)	% Yield isolated	
benzylidene- malononitrile	2	2	0.2	ambient	0.17	0.5	77	a
	2	2	0	25°	16.8	9.1	84	a
cyclohexylidene- malononitrile	2	2	0.2	ambient	0.17	0.5	71	b
	2	2	0	ambient	1.0	7.5	68	b
ethyl benzylidene- cyanoacetate	2	2	0.2	ambient	0.2	0.5	81	c
	2	2	0	25°	144	-	46	c
ethyl benzylmalonate	2	2	0.2	reflux	96	-	33	d
	2	2	0	reflux	96	-	0	d

a : benzaldehyde as substrate with malononitrile as reactant

b : cyclohexanone as substrate with malononitrile as reactant

c : benzaldehyde as substrate with ethyl cyanoacetate as reactant

d : benzaldehyde as substrate with diethyl malonate as reactant

\* : time for initial base peak area to decrease by 50%



Rand<sup>35</sup> conducted similar reactions using potassium fluoride as the basic catalyst in benzene. However, the reactions required heating at 60° C for periods of six to twenty-four hours except for malononitrile condensed with benzaldehyde at 25° C. The reaction of diethyl malonate with benzaldehyde at 60° C for twenty-four hours yielded no isolated products. The reaction times for the reactions carried out by Rand were longer than the reaction times required when 18-crown-6 was present. The yields, though, when 18-crown-6 was present are comparable to the yields obtained by Rand, as well as, by other synthetic routes except for the diethyl malonate condensation.

Aoyama<sup>30</sup> obtained ethyl benzylidenecyanoacetate in 75% yield from condensing ethyl cyanoacetate and benzaldehyde (R/S ratio 1:1) in refluxing ethanol for one hour with potassium fluoride as catalyst. Pratt<sup>151</sup> has obtained the following benzylidenemalononitrile, ethyl benzylidenecyanoacetate, and ethyl benzalmalonate with yields of 74%, 72%, and 89%, respectively. Pratt carried out these reactions with an R/S ratio of one to one (1:1) in refluxing benzene with piperidine and caproic acid present and continually removing water from the system. Cope<sup>139</sup> similarly obtained cyclohexylidenemalononitrile in 80% yield from condensing malononitrile and cyclohexanone (R/S ratio 1:1) with piperidine as the base.

The shorter reaction times noted in the Knoevenagel reactions in the presence of 18-crown-6 was undoubtedly related to the increase in the solubility of potassium fluoride and ion

pair dissociation. With an increase in the concentration of potassium fluoride in solution, an increased concentration of "naked" fluoride ions was expected since 18-crown-6 increases ion pair dissociation. This increase in "naked" fluoride ion concentration can be expected to increase the concentration of the carbanion of the active methylene compound. This increase of the carbanion concentration should shift the equilibrium toward addition across the carbonyl followed by dehydration to the double bond adduct.

#### Alkylations

The alkylations were carried out in acetonitrile using benzyl bromide, benzyl chloride, and methyl iodide as substrates with diethyl malonate as the reactant. The R/S ratio was maintained at one to one (1:1). The results are tabulated in Table 5.

Examination of Table 5 reveals that the reactions carried out in the presence of 18-crown-6 has better yields than the reactions without 18-crown-6. The reactions involving the benzyl halides yielded no isolated products when 18-crown-6 was not present. The half-times ( $t_{1/2}$ ) for these two reactions show the bromide was displaced by diethyl malonate carbanion more readily than the chloride. This was the expected order of leaving group abilities. However, the displacement of iodide from methyl iodide by the diethyl malonate carbanion was extremely slow as noted by the length of time required for the reaction. There is no experimental evidence available, as

Table 5. Alkylations Initiated by Potassium Fluoride in the Presence and Absence of 18-Crown-6

Product	Substrate Conc. (M)	Reactant Conc. (M)	Crown Conc. (M)	Temperature °C	Time (hr)	t <sub>1/2</sub> * (min.)	% Yield isolated	
diethyl	1.2	1.2	0.12	25	41	7.4	63	a
benzylmalonate	1.2	1.2	0	25	41	-	0	a
	1.2	1.2	0.12	25	186	49.5	56	b
	1.2	1.2	0	25	186	-	0	b
diethyl	1.2	1.2	0.12	25	41	7.4	12	a
dibenzyl-	1.2	1.2	0	25	41	-	0	a
malonate	1.2	1.2	0.12	25	186	49.5	10	b
	1.2	1.2	0	25	186	-	0	b
diethyl	2.5	2.6	0.26	25	1392	-	53	c
methylmalonate	2.5	2.6	0	25	1392	-	26	c

a : benzyl bromide as substrate and diethyl malonate as reactant  
b : benzyl chloride as substrate and diethyl malonate as reactant  
c : methyl iodide as substrate and diethyl malonate as reactant

yet, to explain this anomaly. In both cases with the benzyl halide, monoalkylated and dialkylated products were isolated in similar yields. In the case of methyl iodide, only the monoalkylated product was isolated with no evidence of dialkylated product. Overall, though, the yields of the alkylated products compare favorably to other synthetic routes.

Sen<sup>141</sup> found diethyl malonate reacted with benzyl chloride (R/S ration 1:1) in dry ethanol with anhydrous potassium carbonate and potassium fluoride as the base. The only product isolated from the reaction was the monosubstituted product, diethyl benzylmalonate (64%). The reaction mixture was heated to reflux for eight hours. The need for the potassium carbonate used in the reaction was not made clear.

Leucks<sup>152</sup> isolated diethyl benzylmalonate (85%) and diethyl dibenzylmalonate (12%) from reacting diethyl malonate and benzyl chloride (R/S ratio 2:1) in absolute ethanol in the presence of sodium. Similarly, Marvel<sup>153</sup> isolated diethyl benzylmalonate (51-57%) and some diethyl dibenzylmalonate by reacting diethyl malonate and benzyl chloride (R/S ratio 1:1) in refluxing absolute ethanol with sodium. Olivier<sup>154</sup> isolated diethyl methylmalonate (80%) and some diethyl dimethylmalonate by reacting diethyl malonate and methyl iodide (R/S ratio 1:1) in refluxing absolute ethanol with sodium.

#### 18-Crown-6 Complexes

In the course of this research three novel non-metallic

18-crown-6 complexes were isolated, see Table 6. These complexes were formed with cyanogen bromide, malononitrile, and succinonitrile. The cyanogen bromide complex slowly decomposed out of solution with the loss of cyanogen bromide, as noted by the analytical data indicating low nitrogen and bromide content for a two to one complex (cyanogen bromide to 18-crown-6 molar ratio). The analytical data for the malonitrile and succinonitrile complexes agreed with the calculated values for a two to one complex (nitrile to 18-crown-6 molar ratio). Each complex, however, did have a higher melting point than the corresponding melting point for each constituent composing the complexes.

Single crystal x-ray analysis of the cyanogen bromide/18-crown-6 has shown the complex to definitely be a two to one complex as depicted in Figures 1 and 2. From the x-ray structure, the cyanogen bromide molecules were found to be located above and below the 18-crown-6 ring which was planar. The cyanogen bromide molecules were oriented with the bromide moiety aligned toward the center of the 18-crown-6 ring. Neither bromide moiety was directly inserted in the hole of the 18-crown-6 ring unlike the complexes formed by Cram<sup>101</sup> with p-toluene-diazonium tetrafluoroborate and 18-crown-6. Cram<sup>+</sup> postulated the complexes involved insertion of the linear -N=N- group into the hole of 18-crown-6 based on PMR shifts.

Differential thermal analysis (DTA) and thermogravimetric analysis (TGA)<sup>153</sup> was carried out on the malononitrile

Table 6. Elemental Analysis of 18-Crown-6 Complexes

Complex	Complex Formula	MP (C°)	Elemental Analysis					
			%C	%H	%N	%O	%Br	
Cyanogen bromide	C <sub>12</sub> H <sub>28</sub> O <sub>6</sub> (CNBr) <sub>2</sub>	64.5-	35.61	5.08	5.89	20.15	33.57	a
		68.0	38.45	5.81	5.02	22.33	28.39	b
Malononitrile	C <sub>12</sub> H <sub>24</sub> O <sub>6</sub> (C <sub>3</sub> H <sub>2</sub> N <sub>2</sub> ) <sub>2</sub>	127.0-	54.43	7.12	14.14	24.21	-	a
		129.0	54.47	7.14	14.16	24.23	-	b
Succinonitrile	C <sub>12</sub> H <sub>24</sub> O <sub>6</sub> (C <sub>4</sub> H <sub>4</sub> N <sub>2</sub> ) <sub>2</sub>	83-	56.55	7.60	22.62	13.20	-	a
		84	57.06	7.68	21.98	13.28	-	b

a : calculated  
b : experimental

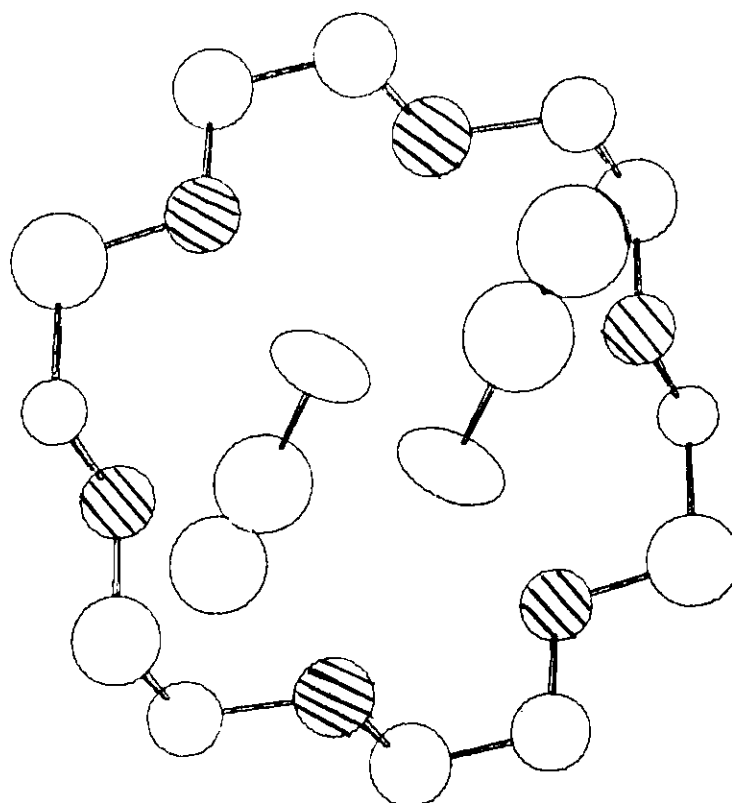



Figure 1. Overview of Cyanogen Bromide/18-Crown-6 Complex

Oxygen : 

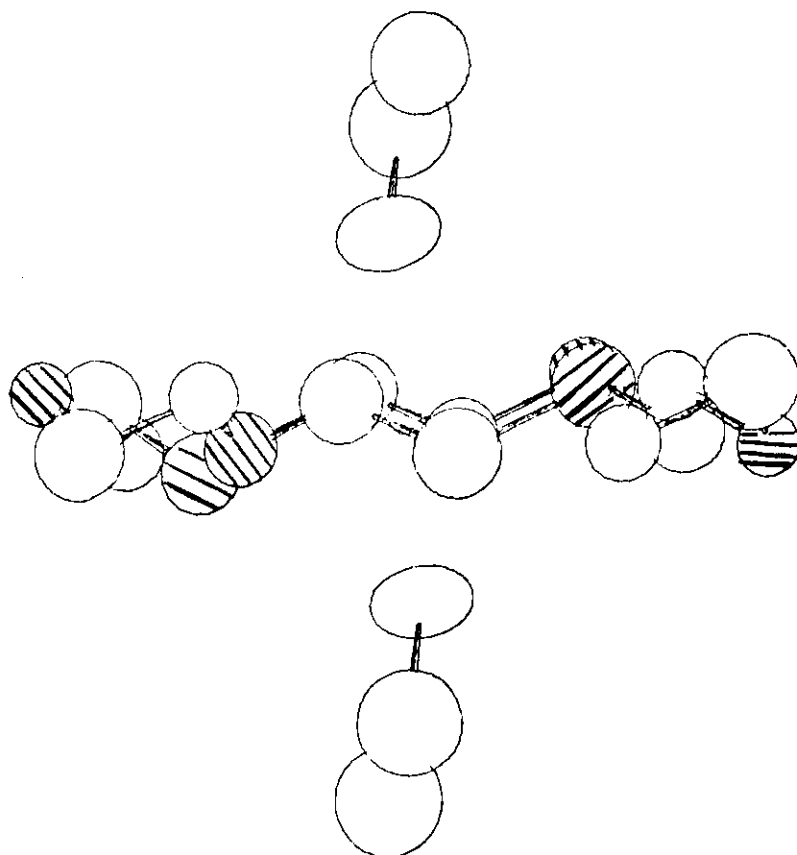
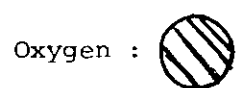


Figure 2. Sideview of Cyanogen Bromide/18-Crown-6 Complex





and succinonitrile complexes. In both cases no endothermic or exothermic transitions were found before the endotherm associated with melting. The DTA/TGA data showed negligible weight losses over the temperature range to melting. The temperature where melting occurred, obtained by DTA for the malonitrile and succinonitrile complexes was 130° C and 87° C, respectively, agreeing with capillary tube melting points.

The nitrile absorption in the infrared region 2200-2250  $\text{cm}^{-1}$  showed a shift to lower values when the nitriles were complexed. Malonitrile shifted from 2251  $\text{cm}^{-1}$  on complexation and succinonitrile shifted from 2226  $\text{cm}^{-1}$  to 2221  $\text{cm}^{-1}$  on complexation. Such shifts indicate some weakening in bond strength of the nitrile triple bond, although the shifts are small. Small shifts were also noted in the  $^{13}\text{C}$ -NMR for the complexes for the 18-crown-6 carbons and nitrile carbon when compared to the individual constituents of the complexes. The shifts indicated some degree of association in solution although no quantitative results were obtained.

No bonding scheme has been established for the complexes. However, these complexes can be recrystallized. This indicates a strong affinity between the 18-crown-6 and the nitrile functionality in non-polar solvents.

## CHAPTER IV

## CONCLUSIONS

When potassium fluoride was solubilized by 18-crown-6 in the polar and nonpolar aprotic solvents, acetonitrile and benzene, the "naked" fluoride ions proved to be effective as a base capable of catalyzing Michael, Knoevenagel, and alkylation reactions. The 18-crown-6 was present only in catalytic quantities. The reaction times for the reactions with 18-crown-6 present were shorter than when 18-crown-6 was not present. The yields of products were comparable to the yields obtained by other standard methods.

Cyanogen bromide, malononitrile, and succinonitrile form a two to one molar complex with 18-crown-6. The malononitrile and succinonitrile complexes were stable melting at 127-129<sup>o</sup> C and 83-84<sup>o</sup> C, respectively.

## CHAPTER V

## RECOMMENDATIONS

Further studies in the use of the fluoride anion as a base in the field of weak-base-promoted reactions should prove interesting. In association with these studies, other polar aprotic solvents should be studied as possible solvents. Such solvents which would be of interest are DMF, N-methylpyrrolidine, DMSO, or HMPA. These solvents with 18-crown-6 may increase the fluoride solubility and decrease reaction time.

X-ray crystallography should be conducted on the 18-crown-6/nitrile complexes to determine their structure and provide insight into the reason for such complex formation. Consideration should be given to attempts at forming the complexes with the halide derivatives of the nitriles if x-ray crystallographic analysis fails for the light atom complexes.

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